



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b>  <b>G01N 1/28, 1/04</b>	<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 99/44063</b>  <b>(43) International Publication Date:</b> 2 September 1999 (02.09.99)
<b>(21) International Application Number:</b> PCT/US99/04001  <b>(22) International Filing Date:</b> 24 February 1999 (24.02.99)  <b>(30) Priority Data:</b> 60/075,979                      25 February 1998 (25.02.98)                      US  <b>(71) Applicant (for all designated States except US):</b> THE UNITED STATES OF AMERICA, represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; National Institutes of Health, Office of Technology Transfer, Suite 325, 6011 Executive Boulevard, Rockville, MD 20852-3804 (US).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> LEIGHTON, Stephen, B. [US/US]; 9007 Woodland Drive, Silver Spring, MD 20910 (US). KONONEN, Juha [FI/US]; 1920 Valley Stream Drive, Rockville, MD 20851 (US). KALLIONIEMI, Olli [FI/US]; 1083 Grand Oak Way, Rockville, MD 20852 (US).  <b>(74) Agent:</b> NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Winston, LLP, Suite 1600 - One World Trade Center, 121 S.W. Salmon Street, Portland, OR 97204 (US).		<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>  <b>(88) Date of publication of the international search report:</b> 4 November 1999 (04.11.99)
<b>(54) Title:</b> TUMOR TISSUE MICROARRAYS FOR RAPID MOLECULAR PROFILING  <b>(57) Abstract</b>  <p>An array-based technology facilitates rapid correlated gene copy number and expression profiling of a very large numbers of human tumors. Hundreds of cylindrical tissue biopsies (diameter 0.6 mm) from morphologically representative regions of individual tumors can be arrayed in a single paraffin block. Consecutive sections from such arrays provide targets for parallel in situ visualization and quantitation of DNA, RNA or protein targets. For example, amplifications of six loci (mybL2, erbB2, Cyclin-D1, myc, 17q23 and 20q13) were rapidly determined by fluorescence in situ hybridization from 372 ethanol-fixed breast cancers. Stratification of tumors by estrogen receptor and p53 expression data revealed distinct patterns of gene amplification in the various subgroups of breast cancer that may have prognostic utility. The tissue array technology is useful in the rapid molecular profiling of hundreds of normal and pathological tissue specimens or cultured cells.</p>		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon	KR	Republic of Korea	PL	Poland		
CN	China	KZ	Kazakhstan	PT	Portugal		
CU	Cuba	LC	Saint Lucia	RO	Romania		
CZ	Czech Republic	LI	Liechtenstein	RU	Russian Federation		
DE	Germany	LK	Sri Lanka	SD	Sudan		
DK	Denmark	LR	Liberia	SE	Sweden		
EE	Estonia			SG	Singapore		

## INTERNATIONAL SEARCH REPORT

Int. uonal Application No. PCT/US 99/04001

## A. CLASSIFICATION OF SUBJECT MATTER

G 01 N 1/28, G 01 N 1/04

According to International Patent Classification (IPC) or to both national classification and IPC

6

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G 01 N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4914022 A (FURMANSKI et al.) 03 April 1990, fig. 1a, column 1, lines 62-64, column 2, lines 35-40, column 3, lines 27-30. Claims 1,2,4-6.	27
A		1-3, 6,7,9, 10-13, 15,16
A	GB 2197471 A (DEREK RICHARD GADSON) 18 May 1988, page 1, line 1 - page 3, line 85.	1, 6-13
A	US 4820504 A	1,3,7,



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

18 June 1999

Date of mailing of the international search report

24.08.99

Name and mailing address of the ISA

European Patent Office, P.O. 5818 PatentAan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

MOSSER e.h.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/04001

-2-

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>(BATTIFORA) 11 April 1989, claims 1-7, 10, 13-16, 20-37.</p> <p>--</p> <p>EP 0332322 A2 (ELSEVIER SCIENCE PUBLISHING CO., INC.) 13 September 1989, abstract, fig. 1, claim 1.</p> <p>----</p>	<p>9-13, 16, 27- 30</p> <p>24-26</p>

# ANHANG

zum internationalen Recherchen-  
bericht über die internationale  
Patentanmeldung Nr.

# ANNEX

to the International Search  
Report to the International Patent  
Application No.

# ANNEXE

au rapport de recherche inter-  
national relatif à la demande de brevet  
international n°

PCT/US 99/04001 SAE 227251

In diesem Anhang sind die Mitglieder  
der Patentfamilien der im obenge-  
nannten internationalen Recherchenbericht  
angeführten Patentdokumente angegeben.  
Diese Angaben dienen nur zur Unter-  
richtung und erfolgen ohne Gewähr.

This Annex lists the patent family  
members relating to the patent documents  
cited in the above-mentioned inter-  
national search report. The Office is  
in no way liable for these particulars  
which are given merely for the purpose  
of information.

La présente annexe indique les  
membres de la famille de brevets  
relatifs aux documents de brevets cités  
dans le rapport de recherche inter-  
national visée ci-dessus. Les renseigne-  
ments fournis sont donnés à titre indica-  
tif et n'engagent pas la responsabilité  
de l'Office.

In Recherchenbericht angeführtes Patentdokument Patent document cited in search report Document de brevet cité dans le rapport de recherche		Datum der Veröffentlichung Publication date Date de publication	Mitglied(er) der Patentfamilie Patent family member(s) Membre(s) de la famille de brevets	Datum der Veröffentlichung Publication date Date de publication
US A	4914022	03-04-1990	keine - none - rien	
GB A1	2197471	18-05-1988	GB A0	8626920
			GB A0	8725600
US A	4820504	11-04-1989	AT E	91788
			AU A1	68697/87
			AU B2	606329
			CA A1	1295218
			DE C0	3786572
			DE T2	3786572
			DK A0	687/87
			DK A	687/87
			EP A2	238190
			EP A3	238190
			EP B1	238190
			ES AF	2004874
			FI A0	870578
			FI A	870578
			IL A0	81529
			JP A2	63132163
			NO A0	870535
			NO A	870535
			NZ A	219237
			PT A	84369
			ZA A	8700925
EP A2	332322	13-09-1989	JP A2	2008959
			US A	4945476